# WEST Search History

DATE: Tuesday, October 29, 2002

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| L2 | L1 and pylori | 24 | L2 |
| L3 | 6290962.pn. and step | 1 | L3 |

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# WEST Search History

DATE: Tuesday, October 29, 2002

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END OF SEARCH HISTORY

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removal, customized scheduling. See HELP ALERT.
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See Help News50 for details.
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  File  65:Inside Conferences  1993-2002/Oct W4
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*File 128: New Major Event category is introduced. See Help News128
for further information.
  File  16:Gale Group PROMT(R)  1990-2002/Oct 25
         (c) 2002 The Gale Group
*File  16: Alert feature enhanced for multiple files, duplicate
removal, customized scheduling. See HELP ALERT.
  File 348:EUROPEAN PATENTS  1978-2002/Oct W03
         (c) 2002 European Patent Office

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S1        138   ((RECOMBINA? OR ATTENUAT? OR MUTANT? OR MUTAGEN?) (25N) (S-
              ALMONELL? OR TYPHIMUR? OR TYPHI?)) AND (HELICOBACT? OR PYLORI
              OR PYLORIS OR PYLROIDIS OR PYLROI OR PYLORIDIS OR PYLORIS OR -
              PYLORUM OR HPYLORI OR UREASE?)
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 1/9/18     (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08560347   95317474   PMID: 7796956
  The history of live bacterial vaccines.
  Lindberg A A
  Lederle-Praxis Biologicals, Wayne, NJ, USA.
  Developments   in   biological   standardization (SWITZERLAND)   1995,   84
 p211-9,  ISSN 0301-5149   Journal Code: 0427140
  Document type: Historical Article; Journal Article
  Languages: ENGLISH
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Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Recent developments have made it possible to construct non-reverting live bacterial vaccine candidates with defined deletions of two or more genes. Such vaccines have proven safe and immunogenic in human volunteers. Since the virulent parent strains are only pathogenic to man (S. typhi, S. flexneri, and V. cholerae), they pose no threat to the environment. Besides holding promise as efficacious vaccines for protection against typhoid fever, bacillary dysentery and cholera, the attenuated strains are well suited as vectors for delivery of heterologous antigenic epitopes from micro-organisms such as **Helicobacter pylori** , Neisseira gonorrhoeae, rotavirus, HIV and many others. Instead of using a virulent parent bacterium as the starting organism for making a vector, attempts have recently been made to employ non-pathogenic bacteria of the normal human flora, such as Streptococcus gordonii for delivery of foreign antigens. At present, the feasibility of this approach for human beings remains to be proven.

Tags: Animal; Human

Descriptors: *Bacterial Vaccines--history--HI; Bacterial Infections --history--HI; Bacterial Infections--prevention and control--PC; Bacterial Vaccines--genetics--GE; Genetic Vectors; History of Medicine, 19th Cent.; History of Medicine, 20th Cent.; Mutation; **Salmonella typhi** --genetics --GE; **Salmonella typhi** --immunology--IM; Shigella--genetics--GE; Shigella--immunology--IM; Vaccines, **Attenuated** --history--HI; Vaccines, Synthetic--history--HI; Vibrio cholerae--immunology--IM

CAS Registry No.: 0 (Bacterial Vaccines); 0 (Genetic Vectors); 0 (Vaccines, Attenuated); 0 (Vaccines, Synthetic)

Record Date Created: 19950801

**1/9/19 (Item 19 from file: 155)**
DIALOG(R)File 155:MEDLINE(R)

08435771 95198543 PMID: 7891557

**Non-motile mutants of** Helicobacter pylori **and** Helicobacter **mustelae defective in flagellar hook production.**

O'Toole P W; Kostrzynska M; Trust T J

Department of Biochemistry and Microbiology, University of Victoria, British Columbia, Canada.

Molecular microbiology (ENGLAND) Nov 1994, 14 (4) p691-703, ISSN 0950-382X Journal Code: 8712028

Contract/Grant No.: R01A129927-01A2; PHS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Flagellar hooks were purified from **Helicobacter pylori** and **Helicobacter** mustelae. The 70 x 16 nm H. **pylori** hook was composed of FlgE subunits of 78kDa, while the 72 x 16 nm H. mustelae hook was composed of 87 kDa subunits. N-terminal sequence was obtained for the FlgE proteins of both species, and for an internal H. mustelae FlgE peptide. Degenerate oligonucleotide primers allowed amplification of a 1.2 kb fragment from the H. mustelae chromosome, which carried part of the flgE gene. The corresponding H. **pylori** gene was cloned by immunoscreening of a genomic library constructed in lambda ZAP Express. The translated H. **pylori** flgE sequence indicated a protein with limited homology with the hook proteins from **Salmonella typhimurium** and Treponema phagedenis. **Mutants** of H. **pylori** and H. mustelae defective in hook production generated by allele replacement were non-motile and devoid of flagellar filaments but produced both flagellin subunits, which were localized in the soluble fraction of the cell. The level of flagellin production was unchanged in the mutants, indicating that the regulation of flagellin expression in **Helicobacter** differs from that in the Enterobacteriaceae.

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: Flagella--ultrastructure--UL; * **Helicobacter** --genetics--GE; * **Helicobacter** --ultrastructure--UL; * **Helicobacter pylori** --genetics --GE; * **Helicobacter pylori** --ultrastructure--UL; *Mutation; Amino Acid

Language: English Record Type: Fulltext
Document Type: Newsletter; Professional Trade
Word Count: 427
TEXT:
J.P. Krachenbuhl. Institute of Experimental Cancer Research and Institute of Biochemistry, University of Lausanne, France.

According to an abstract submitted by the authors to the 4th International Conference on the Prevention of Infection, held May 6-7, 1996, in Nice, France, "The ideal vaccine as defined by WHO should have the following properties: cost effectiveness ((approx)50 cents a dose) long lasting protection, mucosal administration as a unique dose given preferentially in the first year of age, and no requirement for a cold chain. This is a real challenge for the scientists. Recombinant DNA technology linked to a better understanding of host-microbial interactions and molecular and cellular mechanisms of the host response have revolutionized the field of vaccinology and should contribute to the design of ideal vaccines. In mucosal vaccinology, however, progress has been hampered by the difficulty to deliver vaccine carriers by the oral route and by difficulties in assessing immune responses in the mucosal environment. Many microorganisms invade and infect the host via mucosal surfaces by crossing the tight epithelial barrier of the gut, the airways or the urogenital tract. They usually exploit the antigen sampling cells of the mucosal immune system. Resident specialized epithelial cells, the so-called M cells present in the follicle-associated epithelium of mucosa-associated lymphoid tissue act as a portal of entry for pathogenic viruses, bacteria and parasites. In stratified and simple epithelia, uptake of microorganisms is mediated by non epithelial cells, the dendritic of Langerhans cells that are to migrate to local or distant lymphoid tissue, thus facilitating systemic spread of the infectious agents. Theses considerations are important for the design of mucosal vaccines. Vaccines that have to be administered by mucosal routes (oral, nasal, rectal or vaginal) have to reach the antigen sampling sites, cross the epithelial barrier, and enter lymphoid tissue where they can be seen by the immune system. We have designed a subunit vaccine against a pathogen. **Helicobacter pylori** responsible for chronic atrophic gastritis in humans, ulcer disease, and gastric carcinomas and lymphomas. **Helicobacter pylori** survives in the stomach due to its **urease** activity. Recombinant **urease** and cholera or labile toxin as mucosal adjuvant, administered orally elicit an immune response which is both prophylactic and therapeutic in mice. The vaccine is safe in humans and a phase 2 trial with infected volunteers is currently underway in Lausanne. A second generation of vaccine aimed at enhancing the duration of protection has been designed. We have selected live **recombinant Salmonella typhimurium** as a vaccine carrier **attenuated** in its survival in macrophages. The bacterial vaccine is presently tested in mice."


PUBLISHER NAME: Charles W. Henderson
EVENT NAMES: *310 (Science & research)
GEOGRAPHIC NAMES: *4EUFR (France)
PRODUCT NAMES: *2831210 (Vaccines for Human Use)
INDUSTRY NAMES: BUSN (Any type of business); HLTH (Healthcare - Medical and Health)
NAICS CODES: 325412 (Pharmaceutical Preparation Manufacturing)

**1/9/119 (Item 11 from file: 16)**
DIALOG(R)File 16:Gale Group PROMT(R)


04072892 Supplier Number: 45930517 (THIS IS THE FULLTEXT)
**Conference Coverage (ICAAC) New Strategies Revolutionize Vaccinology**
TB Weekly, pN/A
Nov 13, 1995
ISSN: 1065-982X
Language: English Record Type: Fulltext
Document Type: Newsletter; Trade
Word Count: 1717
TEXT:

There will soon be vaccines able to prevent - or even cure - many diseases that have plagued mankind for centuries, an expert vaccinologist predicted.

Recent technological breakthroughs have revolutionized the field of vaccinology, said Stanley Plotkin, a research scientist at the venerable laboratories of Pasteur Merieux, Marnes-la-Coquette, France.

Plotkin made his remarks during an invited lecture to the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), held September 17-20, 1995, in San Francisco, California.

"The field [of vaccinology] has never been in better health," Plotkin said.

In his tour-de-force address, titled "New Techniques for Vaccine Development," Plotkin provided an overview of this relatively new but rapidly expanding field. He observed that while the classical strategy of making vaccines from inactivated organisms continues to bear fruit, it has also given birth to new approaches.

The various strategies based on the old vaccine paradigms include:

* The classical approach of using inactivated whole organisms (examples include intravenous polio vaccine, hepatitis A vaccine, and several bacterial vaccines including the whole-cell pertussis vaccine).

* When organisms produce a single native protein, those have been used in vaccines. Examples include vaccines for diphtheria, tetanus toxoid, hepatitis B [S antigen purified from plasma], and more recently, experimental vaccines based on the **Helicobacter pylori urease** or toxin and excreted proteins of Mycobacterium tuberculosis.

* Experimental vaccines based on capsular polysaccharides, such as those from HIV, pneumococcus, meningococcus, typhoid VI, and group B streptococcus.

* Subunit vaccines, based on immunogenic portions of disease organisms. "Influenza vaccine is essentially a subunit vaccine, so are the newer acellular pertussis vaccines, the cytomegalovirus GB protein-based vaccine, and other experimental vaccines," Plotkin said.

But vaccine development has gone beyond the springboard of the classical strategy to completely novel strategies.

"There is the highly successful use of chemical coupling procedures to change the T-cell-independent polysaccharide vaccines to T-cell-dependent protein vaccines," Plotkin said. "The extension of this principle of conjugation is going quite far."

An example is a vaccine based on the pneumococcal polysaccharide attached to a protein carrier. Other examples include experimental HIV vaccines and pneumococcus and meningococcus A and C conjugate vaccines currently under study. Other vaccines being developed based on this principle include vaccines against staphylococcus and pseudomonas.

New recombinant genetic techniques provide another novel strategy for vaccine development.

"This approach has yielded us hepatitis B vaccines made in yeast, a genetically modified pertussis toxin produced in a recombinant organism and which has recently been licensed in Italy, and the Borrelia bergdorferi outer surface protein A vaccine against Lyme disease now being tested in a Phase III trial," Plotkin said. "However, I would say that surprisingly few vaccines have been developed for this category yet."

Advances in molecular biology permit researchers to create synthetic peptides "off the shelf" by stringing together amino acids in the laboratory.

"So far, although a great deal of work has been done in HIV and malaria, we have not yet got a peptide-based vaccine," Plotkin said. "The reasons for that are that the simple peptide may not be immunogenic because it's dependent on conformation and also [because of the need for improved] adjuvants. It should be mentioned, however, that peptides are being improved by lipidation and other techniques, and therefore may make a leapfrog and we may have vaccines from peptides alone soon."

The need for improved adjuvants goes far beyond their requirement in peptide-based vaccines.

"It is crucial that new adjuvants be licensed to fulfil the promise of subunit, recombinant protein, or subunit vaccines," Plotkin said.

Adjuvants fall into two categories:

* Mechanical adjuvants, which are basically adjuvants that make depots of the antigens and allow slow release to provide local immune stimulation.

* More general adjuvants which stimulate the immune system in general to improve immune responses to injected antigens or to antigens

administered at an earlier time.

Yet another new technique for vaccine development is the creation of the particles that have been dubbed pseudovirions.

"It is now possible to tailor the genomes of viruses so that after transfection into cells structural proteins are synthesized and assembled into pseudoparticles, but without the genes needed to synthesize new virus," Plotkin said.

Other strategies include:

* Anti-idiotypic antibodies. "An idea whose time has not yet come except perhaps in the treatment of B-cell lymphomas," Plotkin said.

* Naked DNA. "An astounding and outstanding advance," Plotkin said (see the accompanying article in this issue).

* Microencapsulization of antigens. "[This technique] has been explored for some time and may be useful both for prolonging release of injected antigens and allowing mucosal immunization if the microparticles are taken up by mucosal cells," Plotkin said. "In addition, work is proceeding on nanoparticles, which are smaller and easily absorbed."

* Live vaccines. "The classical strategies are still bearing fruit," Plotkin noted. "However, attenuation in animals such as was done for yellow fever and rabies is definitely passe. Nevertheless, the Jennerian idea of seeking vaccines from viruses in other species is far from dead. Bovine parainfluenza 3 is a candidate attenuated vaccine, and the rotavirus vaccine started with animal viruses. Attenuation in cell culture, or by passage, has of course given us many vaccines - measles, mumps, oral polio vaccine, most recently varicella vaccine - and today we are working with dengue strains, four serotypes of attenuated dengue viruses which in principle when given together will immunize against all four serotypes and against dengue."

* Attenuation of live vaccines by low-temperature adaptation. "The ability of viruses to grow at low temperatures is a phenotypic characteristic associated generally with attenuation," Plotkin observed. "Induction of that characteristic has been achieved by [adaptation] or by artificially induced mutation. Though not well known, the rubella vaccine was actually attenuated by cold adaptation and today cold-adapted vaccines for influenza, parainfluenza, and RSV [respiratory syncytial virus] are under active tests."

* Attenuation of live vaccines by reassortment. "When the viral genome is segmented, reassortment can be used to create hybrids between the attenuated recipient viruses and immunogenic donor viruses," Plotkin said. "The principle is used every year for flu vaccines and is the basis for the candidate rotavirus vaccine."

* Attenuation of live vaccine organisms by genetic engineering. "The ability of molecular engineering to create new characteristics by deletion and/or by addition of genetic material is being fully explored," Plotkin said. "HIV deletion mutants are being tested for **attenuation** in animals and herpesvirus **mutants** are already being used in animal vaccination. The same principles have been used in bacteriology to develop the **salmonella** TY21A oral typhoid vaccine."

* Novel RNA organisms created by reverse genetics. "A segment of influenza cDNA inserted into a plasmid can be mutated by site-directed mutagenesis and then converted to its corresponding RNA," Plotkin explained. "This RNA can then be transfected into an influenza virus-infected cell. The reassortment process that then occurs is natural, and you can then select for a virus which contains the mutated gene segment. That enables you to determine what the effect of your mutation is - that is, which mutation effects attenuation."

In the final portion of his lecture, Plotkin gazed into his crystal ball to predict the future of immunology.

"What conclusions can we draw for the future? Well, first the classical methods of vaccine development will continue to bear fruit," he said. "Second there is the tendency towards combined vaccines including at least six valences. But I foresee a limit to combinations."

Plotkin noted that even with just six valences a combined vaccine would have an exponentially vast number of individual components for the immune system to deal with, and there are many other valences clinicians would like to add to a pediatric combination.

"Aside from compatibility issues, it is not clear that the immune system can mount optimal responses to multiple antigens," he said. "Already some incompatibility issues have been seen; fortunately of little clinical

consequence. But as the number of antigens in a vaccine increases, the immunogenicity will decrease. In particular there is the problem of antigenic competition. This may arise simply by induction of T suppressor cells or by competition between peptides for MHC molecules, or by carrier induced epitopic suppression, that is, when a carrier protein is used, in which antibody responses to haptens are inhibited by prior immunization with the protein carrier. This is not a theoretical issue: competition has already been noted between HIV and pneumococcal vaccines in clinical trials."

This phenomenon suggests that in the future people will receive vaccinations at various times during their lives, both for boosting of vaccines previously received and for new, age-specific vaccinations.

"A third tendency is that acellular pertussis vaccine will replace whole cell vaccine throughout the world," Plotkin predicted. "Today we know that acellular vaccines are more effective than whole cell vaccines. This fact will influence all countries."

The Pasteur-Merieux researcher predicted that some future vaccines will specifically stimulate cellular, as opposed to humoral, immune responses.

"However important antibodies are, in the more complex diseases CMI [cell-mediated immunity] - in particular CTL [cytotoxic lymphocytes] - is also important," he said. "A vaccine obviously seeks to improve immune responses: type 1 responses driving toward CMI and type 2 responses driving toward antibodies. These two tendencies are more or less the yin and the yang of the immune system. It is likely that we will be using cytokines to drive the immune system in one of these two directions."

Plotkin also predicted that future vaccines will target mucosal immune responses.

"There certainly will be the use of non-parenteral or mucosal immunization to protect against respiratory, gastrointestinal, and sexually transmitted diseases," he said. "A number of attempts are being made to take advantage of the mucosal immune system - or rather mucosal immune systems, because different sites may give different results. No area will be inviolate to the vaccinologist: oral, nasal, rectal, and even vaginal routes may be useful methods of immunization."

Finally, Plotkin predicted that vaccines will be used not only to prevent diseases but also to treat them.

"Vaccines historically have been thought of only as preventives, except for some lay people who have been ahead of us in this regard," he said. "Now scientists are themselves turning towards toward the idea of immunization after an agent has been established, in order to suppress that agent though the generation of an immune response in excess of the natural response to infection. A list of possible targets includes herpes, leprosy, tuberculosis, hepatitis, and HIV." - by Daniel J. DeNoon, Senior Editor



PUBLISHER NAME: Charles W. Henderson
EVENT NAMES: *310 (Science & research)
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PRODUCT NAMES: *2831210 (Vaccines for Human Use); 8000146 (Vaccination & Immunization)
INDUSTRY NAMES: BUSN (Any type of business); HLTH (Healthcare - Medical and Health)
NAICS CODES: 325412 (Pharmaceutical Preparation Manufacturing); 621999 (All Other Miscellaneous Ambulatory Health Care Services)

**1/9/122 (Item 14 from file: 16)**
DIALOG(R)File 16:Gale Group PROMT(R)


03375225 Supplier Number: 44683419 (THIS IS THE FULLTEXT)
**New promise for H** pylori **infection**
Pharmaceutical Business News, pN/A
May 16, 1994
ISSN: 0956-0661
Language: English Record Type: Fulltext
Document Type: Newsletter; Trade
Word Count: 1612

TEXT:
The first biennial conference of the Federation of Infection Societies was held in partnership with the British Society for Gastroenterology in Manchester on 4-6 May.

Manchester - A new dual therapy regime which combines the antibiotic clarithromycin (Klaricid - 500 mg tds) with the proton pump inhibitor omeprazole (40 mg od) is currently the most promising treatment for H **pylori** , said Dr Robert Logan, lecturer in Gastroenterology, University Hospital, Queen's Medical Centre, Nottingham and a member of the Parkside **Helicobacter** Study Group, Central Middlesex and St Mary's Hospitals, London.

He said that clarithromycin was currently the single most effective antibiotic for treating H **pylori** , and explained the advantages of the new dual therapy over existing treatments.

Standard triple therapy (bismuth, metronidazole, plus amoxicillin or tetracycline) was limited by poor compliance, side effects, frequent dosing, and the emergence of metronidazole resistant H **pylori** .

The first dual therapy to be developed had been a combination of omeprazole and amoxicillin, but results had proved inconsistent. Some German studies had shown high eradication rates but research groups in the UK, Ireland, France, Portugal, and Italy had been unable to reproduce the German results, instead finding surprisingly low eradication rates with the amoxicillin regime.

"Our group found that clarithromycin 500 mg thrice daily and omeprazole 40 mg daily for two weeks gave an H **pylori** eradication rate of around 80 per cent which was almost double the eradication rate we were able to achieve with omeprazole (at the same dose) combined with amoxicillin," said Dr Logan. "Other groups using omeprazole, clarithromycin regimes have found equally high eradication rates in comparison to omeprazole/amoxicillin," said Dr Logan. "I believe that clarithromycin is going to be a key element in the treatment of H **pylori** in years to come," said Dr Logan. "Our threshold for treatment will fall and I do not believe it will be long before all patients with H **pylori** will be offered at least one course of treatment," he concluded.

Dr Logan will this week present his latest results on H **pylori** eradication to the Digestive Disease Week Conference of the American Gastroenterology Association, New Orleans, Louisiana (15-18 May 1994).

His randomised, double blind, multi-centre study shows that clarithromycin/omeprazole dual therapy effectively eradicates H **pylori** and prevents recurrence of duodenal ulcers.

Some 148 patients with duodenal ulcer and H **pylori** infection received either 500 mg clarithromycin (thrice daily) or placebo for two weeks. All patients received 40 mg omeprazole daily for four weeks. After four weeks ulcers healed in virtually all patients.

Four to six weeks after finishing therapy, patients treated with clarithromycin/omeprazole dual therapy showed an H **pylori** eradication rate of 83 per cent versus one per cent in those who received placebo plus omeprazole.

Furthermore, six months after treatment, ulcers had recurred in more than half of the placebo/omeprazole patients compared with only four per cent of those treated with clarithromycin/omeprazole dual therapy.

"This trial establishes dual therapy with clarithromycin and omeprazole as an effective treatment regimen for the eradication of H **pylori** and prevention of duodenal ulcer relapse. This new regiment has tremendous implications for the future of ulcer therapy," said Dr Logan, (PBN Vol 9 No 214, page 8).

Live salmonella vaccines finally seem to be fulfilling their promise to provide oral multi-vaccine delivery systems, Dr Carlos Hormaeche, of the University of Cambridge told the FIS meeting.

"We have been working on a new generation of live salmonella vaccines. This is an area that has shown promise for a long time - recently it looks as if it is finally beginning to work and the results are very encouraging," he said.

His team recently succeeded in making an experimental salmonella vaccine which conferred protection against salmonella, tetanus and schistosomiasis with a single oral dose.

"There is a need for new vaccines; traditional vaccines remain limited by cost, by the need for a cold chain, by adverse reactions, and by the requirement for administration by injection," said Dr Hormaeche.

The answer was a delivery system which could administer a **recombinant** antigen once the putative target antigen had been identified. **Salmonella** appeared to be excellent carriers for **recombinant** antigens.

If mice were infected with a small dose of pathogenic **salmonella** such as S **typhimurium** or S enteritidis the **salmonella** multiplied rapidly and within five to six days the liver and spleen contained about 108 **salmonella** and the animals died. The secret of turning these bacteria into a useful vaccine was to **attenuate** them in such a way that they grew very slowly, rather than rapidly.

This could be achieved by means of lesions in genes of the aromatic pathway of the salmonella, forming organisms which required aromatic compounds (p -aminobenzoic acid) for their growth. Since p-aminobenzoic acid is not available in host tissues, these organisms grow very slowly.

"A salmonella with a mutation in any of these genes now requires p-aminobenzoic acid. If you inject it into animals at a dose of about one million the salmonella grow very slowly, come to a juddering halt and are cleared away. During this period something strange happens; the process of clearance leaves the animal with very solid immunity and long lasting protection against re-challenge," said Dr Hormaeche.

Vaccines produced this way are called Aro vaccines. They have proved safe and effective in mice, cattle, sheep and chickens and are currently undergoing promising Phase I trials in humans as candidate "new generation" live oral typhoid vaccines. They can elicit humoral, cell mediated and secretory immune responses to recombinant antigens from bacteria, viruses and parasites, said Dr Hormaeche.

Travellers diarrhoea responds to a single tablet of the quinolone ciprofloxacin, reported Dr Imroz Salam and colleagues from the gastroenterology departments at Queen Elizabeth Military Hospital, Woolwich and St Bartholomew's Hospital, London.

They studied British troops deployed in Belize. Soldiers who presented with acute diarrhoea within 24 hours of onset were randomised to 500mg ciprofloxacin or placebo. Subjects recorded the number, consistency of stools and the presence of associated symptoms such as cramps or anorexia for 72 hours or until recovery.

Treatment with ciprofloxacin more than halved the mean duration of diarrhoea (from about 50 hours in the placebo group to 20 in the active) and mean number of liquid stools (from 11 in the placebo group to 5 in the treated group).

"Travellers diarrhoea is the most common illness affecting people travelling across national boundaries. A single dose of ciprofloxacin is effective in reducing both the duration and severity of illness in travellers diarrhoea. It is a simple regime for empirical therapy and is likely to ensure full compliance, reducing the cost and duration of therapy. Such a regime is also unlikely to cause any serious side effects," said Dr Salam.

"However before one universally recommends this regime one has to keep in mind the disturbing reports of ciprofloxacin resistance that have emerged in developing countries. I think we have to determine the mechanisms and prevalence of ciprofloxacin resistance in such areas," he added.

Treatment using omeprazole appears to be associated with an increased risk of Campylobacter infection, according to Dr Keith Neal, of the University of Nottingham Medical School.

The same risk of Campylobacter infection was not seen with H2 antagonists or previous gastric surgery, according to a survey which used statutory notifications Campylobacter food poisoning and general practice records to perform a case-control study.

Records of 147 cases of Campylobacter infection all aged 45 or more years and 294 age, sex and practice matched control subjects were examined. Overall, cases (59 per cent) were slightly more likely than controls (51 per cent) to be receiving regular prescription drugs ($p = 0.15$).

In the month prior to a case's infection 7 cases and one control had been prescribed omeprazole (RR 15.5, $p=0.012$). A weak non-significant association was seen with H2 antagonists prescribed in the month prior to infection. The results were supported by a post marketing surveillance study of patients taking omeprazole long-term (n=1600) which confirmed the increased risk with omeprazole (odds ratio 4.3, 0.00005). "These results are consistent with in vitro data indicating that Campylobacter survival is dependent on a higher pH than salmonella," concluded the Nottingham

researchers.

Toxic megacolon complicating pseudomembranous colitis with a fatal outcome may be more common than has previously been appreciated and could be on the increase with more widespread use of broad spectrum antibiotics in elderly patients, warned Dr Elizabeth Williams and colleagues from the Royal Bournemouth Hospital.

They reported two recent cases in elderly male patients following treatment with a variety of antibiotics. The first patient had diarrhoea and probable bronchopneumonia treated by Septrin and Cefaclor at home and developed constipation in the hospital. He had two negative Clostridium difficile cultures and barium enema before he received treatment with broad spectrum antibodies (including cephalosporins) in the hospital. He developed toxic megacolon requiring subtotal colectomy, C difficile with toxin were isolated and he died within 48 hours of the operation. In the second case the diagnosis was made at autopsy. The patient, admitted with immobility secondary to arthritis and leg ulceration, was treated with six different antibiotics within 18 days.

"Toxic megacolon is a recognised but rarely seen complication of pseudomembranous colitis. Our recent experience may indicate that it is more common than has been appreciated and one might expect the numbers of cases to increase if the widespread use of broad spectrum antibiotics (especially cephalosporins in the elderly) continues," said Dr Williams.

n Formed in 1993, The Federation of Infection Societies (FIS) comprises the British Society for Antimicrobial Chemotherapy, the Association of Medical Microbiologists, the Clinical Infection Society, the British Society for the Study of Infection and the Hospital Infection Society.



PUBLISHER NAME: Financial Times Group
EVENT NAMES: *310 (Science & research)
GEOGRAPHIC NAMES: *4EUUK (United Kingdom)
PRODUCT NAMES: *2834500 (Digestive & Genito-Urinary Preps)
INDUSTRY NAMES: BUSN (Any type of business); DRUG (Pharmaceuticals and Cosmetics); INTL (Business, International)
NAICS CODES: 325412 (Pharmaceutical Preparation Manufacturing)
?t s1/3,kwic/38 39 40 41 42 100 137

**1/3,KWIC/38 (Item 17 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0205672 DBR Accession No.: 97-00793 PATENT
**Expression of genes in animal cells - eukaryote DNA cassette expression in e.g. Yersinia, Escherichia, Neisseria, Aeromonas, and Franciesella spp., and intranasal delivery to mammal cell, for use as a live recombinant vaccine**
AUTHOR: Powell R J; Lewis G K; Hone D M
CORPORATE SOURCE: Baltimore, MD, USA.
PATENT ASSIGNEE: Univ.Maryland-Baltimore-County 1996
PATENT NUMBER: WO 9634631 PATENT DATE: 961107 WPI ACCESSION NO.: 96-518293 (9651)
PRIORITY APPLIC. NO.: US 433790 APPLIC. DATE: 950503
NATIONAL APPLIC. NO.: WO 96US5326 APPLIC. DATE: 960424
LANGUAGE: English

...ABSTRACT: Escherichia, Klebsiella, Bordetella, Neisseria, Aeromonas, Franciesella, Corynebacterium, Citrobacter, Chlamydia, Haemophilus, Brucella, Mycobacterium, Legionella, Rhodococcus, Pseudomonas, **Helicobacter** , Salmonella, Vibrio, Bacillus, Leishmania, and Erysipelothrix spp. which have been genetically engineered to mimic the ...

DESCRIPTORS: ...Escherichia, Klebsiella, Bordetella, Neisseria, Aeromonas, Franciesella, Corynebacterium, Citrobacter, Chlamydia, Haemophilus, Brucella, Mycobacterium, Legionella, Rhodococcus, Pseudomonas, **Helicobacter** , **Salmonella** , Vibrio, Bacillus, Leishmania, Erysipelothrix spp., intranasal delivery to mammal cell, appl. live **recombinant** vaccine bacterium animal (Vol.16, No.2)

**1/3,KWIC/39 (Item 18 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0205060 DBR Accession No.: 97-00181 PATENT
**New** Helicobacter **antigenic preparation - recombinant antigen production by vector plasmid expression in Escherichia coli, and corresponding monoclonal antibody, for application as a recombinant vaccine**
AUTHOR: Doidge C V; Lee A; Radcliffe F J; Hocking D M; Webb E A
CORPORATE SOURCE: Parkville, Victoria, Australia; Kensington, New South Wales, Australia.
PATENT ASSIGNEE: CSL; Univ.New-South-Wales 1996
PATENT NUMBER: WO 9633220 PATENT DATE: 961024 WPI ACCESSION NO.: 96-485735 (9648)
PRIORITY APPLIC. NO.: AU 967565 APPLIC. DATE: 960116
NATIONAL APPLIC. NO.: WO 96AU225 APPLIC. DATE: 960419
LANGUAGE: English

**New** Helicobacter **antigenic preparation**
...ABSTRACT: are claimed: 1) an antigen preparation (AP), for use in the treatment of prevention of **Helicobacter** sp. infection in a human host, comprising antigens of mol.wt. 19,000 (a), 13...

...000 (d), and 29,000 (e), respectively (the preparation may also comprise at least one **Helicobacter pylori** or **Helicobacter** felis antigen); 2) antigens (a)-(e); 3) a vaccine comprising an immunologically effective amount of...

... molecule of 7); 9) Escherichia coli transformed with the vector of 8); and 10) a **recombinant** polypeptide expressed in the host cell of 9). Nucleic acids may be used in plasmids as vaccine vectors ( **Salmonella** , Shigella, Yersinia, Vibrio, Escherichia, or BCG) expressing the antigens in a host. (86pp)
DESCRIPTORS: **Helicobacter** sp. recombinant antigen prep., vector plasmid expression in Escherichia coli, monoclonal antibody, appl. recombinant vaccine...

**1/3,KWIC/40 (Item 19 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0188790 DBR Accession No.: 95-13795 PATENT
**Composition for treating** Helicobacter **infection -** Helicobacter pylori recombinant urease **monoclonal antibody administered using e.g.** Salmonella typhimurium , **Bacillus sp., yeast or herpes virus vector, for gastroduodenal disease therapy**
AUTHOR: Michetti P; Corthesy-Theulaz I; Blum A; Davin C; Haas R; Kraehen-Buhl J P; Saraga E
PATENT ASSIGNEE: Oravax 1995
PATENT NUMBER: WO 9522987 PATENT DATE: 950831 WPI ACCESSION NO.: 95-320292 (9541)
PRIORITY APPLIC. NO.: US 200346 APPLIC. DATE: 940223
NATIONAL APPLIC. NO.: WO 95US2202 APPLIC. DATE: 950223
LANGUAGE: English

**Composition for treating** Helicobacter **infection -** Helicobacter pylori recombinant urease **monoclonal antibody administered using e.g.** Salmonella typhimurium , **Bacillus sp., yeast or herpes virus vector, for gastroduodenal disease therapy**
ABSTRACT: The following are claimed: (1) the use of a composition, containing **Helicobacter** sp. **urease** (EC-3.5.1.5) peptide (I), in the production of a medicament for the...
... a gastroduodenal disease in a mammal; (2) the use of a monoclonal antibody which recognizes **Helicobacter urease** ; and (3) compositions containing the ureB subunit of **Helicobacter pylori urease** , a mucosal adjuvant and hydroxyapatite, and containing the ureB subunit in the form of a...

... genetically linked to the cholera toxin B subunit. Preferably, the composition is contained in a **recombinant** live vector, or a **recombinant** carrier system which expresses **Helicobacter urease** . The live vector is selected from **Salmonella typhimurium** , **Salmonella typhi** , Shigella sp., Bacillus sp., Lactobacillus sp., Mycobacterium bovis BCG, Escherichia coli, Vibrio cholerae, Campylobacter sp...
DESCRIPTORS: **Helicobacter pylori recombinant urease** monoclonal antibody comp., e.g. **Salmonella typhimurium** , **Salmonella typhi** , Shigella sp., Bacillus sp., Lactobacillus sp., yeast, herpes virus, adeno virus, polio virus vector, appl...

**1/3,KWIC/41 (Item 20 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0177044 DBR Accession No.: 95-03865 PATENT
Salmonella **vaccine containing cells** attenuated **by mutation -** recombinant Salmonella **sp.** attenuation **by PhoP regulon and aromatic amino acid synthesis gene virulence-** attenuating **mutation; application in live** recombinant **vaccine**
AUTHOR: Miller S I; Mekalanos J J
PATENT ASSIGNEE: Gen.Hosp.Boston; Harvard-Coll. 1995
PATENT NUMBER: WO 9502048 PATENT DATE: 950119 WPI ACCESSION NO.: 95-066894 (9509)
PRIORITY APPLIC. NO.: US 271354 APPLIC. DATE: 940706
NATIONAL APPLIC. NO.: WO 94US7658 APPLIC. DATE: 940707
LANGUAGE: English

Salmonella **vaccine containing cells** attenuated **by mutation -** recombinant Salmonella **sp.** attenuation **by PhoP regulon and aromatic amino acid synthesis gene virulence-** attenuating **mutation; application in live** recombinant **vaccine**
ABSTRACT: A vaccine is claimed which consists of a bacterial cell in which virulence has been **attenuated** . Also new are: i. vaccines containing **Salmonella** cells **attenuated** by decreased expression of a virulence gene controlled by a phoB regulator; ii. bacteria constitutively...
DESCRIPTORS: recombinant Salmonella sp. construction, **attenuation** , PhoP regulon, aromatic amino acid synth. gene virulence- **attenuating** mutation, appl. live **recombinant** vaccine prep. **Salmonella typhi** **Salmonella** enteriditis **Salmonella** chlorea-suis **Salmonella** pylori **Salmonella** paratyphi pagD envE msgA envF prgH-K bacterium DNA sequence protein sequence (Vol.14, No...

**1/3,KWIC/42 (Item 21 from file: 357)**
DIALOG(R)File 357:Derwent Biotech Res.


0158237 DBR Accession No.: 94-00788 PATENT
**Growth of bacterium cells and selection of mutants -** Salmonella , **Yersinia, Shigella, Campylobacter,** Helicobacter , **Pseudomonas, Streptococcus, etc.; pot. vaccine production, diagnosis,** recombinant **protein production**
PATENT ASSIGNEE: Microcarb 1993
PATENT NUMBER: WO 9322423 PATENT DATE: 931111 WPI ACCESSION NO.: 93-368782 (9346)
PRIORITY APPLIC. NO.: US 875510 APPLIC. DATE: 920429
NATIONAL APPLIC. NO.: WO 93US4053 APPLIC. DATE: 930429
LANGUAGE: English

- Salmonella , **Yersinia, Shigella, Campylobacter,** Helicobacter , **Pseudomonas, Streptococcus, etc.; pot. vaccine production, diagnosis,** recombinant **protein production**
...ABSTRACT: by growing bacteria in the presence of (I). More specifically, the bacterium is selected from **Salmonella** , Yersinia, Shigella, Campylobacter, **Helicobacter** , Pseudomonas, Streptococcus,

Staphylococcus, Escherichia coli, Haemophilus, Mycobacterium, Proteus, Klebsiella, Neisseria, Branhamella, Bacteroides, Listeria, Enterococci, Vibrio, Bordetella, Clostridium, Treponema or Mycoplasma. The **mutant** bacterium may be used for the expression of a cloned DNA molecule. (40pp)
DESCRIPTORS: **Salmonella** , Yersinia, Shigella, Campylobacter, **Helicobacter** , Pseudomonas, Streptococcus, Staphylococcus, Escherichia coli, Haemophilus, Mycobacterium, Proteus, Klebsiella, Neisseria, Bordetella, Clostridium, Treponema, Mycoplasma growth, **mutant** selection, culture medium nutrient comp., pot. vaccine prep., diagnosis, recombinant protein prep. bacterium Branhamella Bacteroides...

**1/3,KWIC/100 (Item 1 from file: 652)**
DIALOG(R)File 652:US Patents Fulltext


00735117
Utility
PROCESS OF SUBJECTING A MICROORGANISM SUSCEPTIBLE MATERIAL TO A MICROORGANISM

PATENT NO.: 3,860,490
ISSUED: January 14, 1975 (19750114)
INVENTOR(s): Guttag, Alvin, Bethesda, MD (Maryland), US (United States of America)
ASSIGNEE(s): National Patent Development Corporation, (A U.S. Company or Corporation ), New York, NY (New York), US (United States of America)
[Assignee Code(s): 58524]
APPL. NO.: 5-347,724
FILED: April 04, 1973 (19730404)

This is a division, of application Ser. No. 225,448 filed Feb. 11, 1972 now U.S. Pat. No. 3767790.

FULL TEXT: 854 lines
... see U.S. Pat. No. 3,226,296), attenuated virus diarrhea virus (Oregon C24V strain) **attenuated** as set forth in U.S. Pat. No. 3,293,129, **attenuated** panleukemia virus (see U.S. Pat. No. 3,293, 130), **attenuated** **Salmonella** dublin (strain ATCC 15480), **attenuated** **Salmonella** gallinarum, noninfectious rinderpest virus (see U.S. Pat. No. 2,756,176), rumen microorganisms, Newcastle virus (9251 strain) **attenuated** by 125 passages in embryonated chicken eggs, see strain of influenza inactivated as set forth...
... membrane consisted of the relatively thick film of cross-linked hydroxyethyl methacrylate polymer containing entrapped **urease** and a relatively thin (0.1 mil) layer of cross-linked hydroxyethyl methacrylate polymer free...

**1/3,KWIC/137 (Item 15 from file: 348)**
DIALOG(R)File 348:EUROPEAN PATENTS


00517596
**Recombinant live vaccines against Gram-negative enteric pathogens**
**Rekombinanter lebender Impfstoff gegen Gram-negative enterische Pathogene**
**Vaccin recombinant vivant contre des agents pathogene enteriques Gram-negatifs**
PATENT ASSIGNEE:
SCHWEIZERISCHES SERUM- & IMPFINSTITUT BERN, (1194260), Postfach 2707, CH-3001 Bern, (CH), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Viret, Jean-Francois, Gartenstrasse 50, CH-3177 Laupen, (CH)
Cryz, Stanly J., Jr., Hosstudenweg 11, CH-3176 Neuenegg, (CH)
Favre, Didier, Pfrunstrasse 28, CH-3176 Neuenegg, (CH)
LEGAL REPRESENTATIVE:

VOSSIUS & PARTNER (100311), Postfach 86 07 67, 81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 564689 A1 931013 (Basic)
EP 564689 B1 970723
APPLICATION (CC, No, Date): EP 92106281 920410;
PRIORITY (CC, No, Date): EP 92106281 920410
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/112; A61K-039/116;
ABSTRACT WORD COUNT: 70

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

| Available Text | Language | Update | Word Count |
|---|---|---|---|
| CLAIMS A | (English) | EPABF1 | 575 |
| CLAIMS B | (English) | 9707W4 | 628 |
| CLAIMS B | (German) | 9707W4 | 576 |
| CLAIMS B | (French) | 9707W4 | 670 |
| SPEC A | (English) | EPABF1 | 12786 |
| SPEC B | (English) | 9707W4 | 12656 |
| Total word count - document A | | | 13362 |
| Total word count - document B | | | 14530 |
| Total word count - documents A + B | | | 27892 |

...SPECIFICATION are shigellosis, typhoid fever, cholera, infections with enterotoxigenic and enteropathogenic Escherichia coli, and infections with **Helicobacter pylori** .

Shigellosis is an acute enteric disease caused by virulent strains of the species Shigella sonnei...S. sonnei rfb/rfc genetic determinant from the whole S. sonnei virulence plasmid in the **attenuated** S. **typhi** /S. sonnei hybrid strain 5076-1C does not lead to the covalent attachment of the corresponding O-antigen onto the S. **typhi** Ra core structure (Seid et al., J. Biol. Chem. 259:9028-9034, 1984). In the...locus, the ilv locus, the viaB locus, or any of the aro loci of S. **typhi** .

Preferred target genes for chromosomal integration via homologous **recombination** into S. **typhi** TY21a may be a chromosomal locus involved in the production of H(sub 2)S...

...expression of complete S. sonnei Form I type LPS molecules may include, without limitation, S. **typhi** or V. cholerae live **attenuated** vaccine strains. Preferred S. **typhi** carrier strain may be the anti-typhoid live vaccine strain TY21a (Germanier and Furer, ibid...

...flexneri, Salmonella typhi, Salmonella enterititis, E. coli being enteropathogenic, enterohemorrhagic, enteroenvasive or enterotoxinogenic, V. cholerae, **Helicobacter pylori** , and Clostridium deficile. Such an invention may also prevent enteric diseases caused by Giardia lambia... weakly), ilvB, ilvG, ilvM, and ilvC, but not ilvD or ilvE E. coli K-12 **mutants** . These results indicate that TY21a is mutated in the ilvD gene encoding dihydroxyacid dehydrase. In both E. coli K-12 and S. **typhimurium** , the ilvD gene belongs to an operon structure (ilvGMEDA operon). It is therefore likely that...

...corresponding ilv locus was cloned from a gene of the chromosomal gene bank of S. **typhi** TY2 described in Example 9 by complementation of the E. coli K-12 ilvC **mutant** strain AB1419. The ilvC locus is adjacent to the ilvGMEDA operon in the E. coli...

...not pILV18, also complemented the ilv defect of both the E. coli K-12 ilvD **mutant** strain AB1280 and S. **typhi** TY21a. This shows that clone pILV12, but not pILV18, most likely includes both the ilvGMEDA...

...SPECIFICATION are shigellosis, typhoid fever, cholera, infections with enterotoxigenic and enteropathogenic Escherichia coli, and infections with **Helicobacter pylori** .

Shigellosis is an acute enteric disease caused by virulent strains of the species Shigella sonnei...S. sonnei rfb/rfc genetic determinant from the whole S. sonnei virulence plasmid in the **attenuated** S. **typhi** /S. sonnei hybrid strain 5076-1C does not lead to the covalent attachment of the corresponding O-antigen onto the S. **typhi** Ra core structure (Seid et al., J. Biol. Chem. 259:9028-9034, 1984). In the...locus, the ilv

locus, the viaB locus, or any of the aro loci of S. **typhi** .

Preferred target genes for chromosomal integration via homologous **recombination** into S. **typhi** TY21a may be a chromosomal locus involved in the production of H2))S (H2))S...

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...flexneri, Salmonella typhi, Salmonella enterititis, E. coli being enteropathogenic, enterohemorrhagic, enteroenvasive or enterotoxinogenic, V. cholerae, **Helicobacter pylori** , and Clostridium deficile. Such an invention may also prevent enteric diseases caused by Giardia lambia... weakly), ilvB, ilvG, ilvM, and ilvC, but not ilvD or ilvE E. coli K-12 **mutants** . These results indicate that TY21a is mutated in the ilvD gene encoding dihydroxyacid dehydrase. In both E. coli K-12 and S. **typhimurium** , the ilvD gene belongs to an operon structure (ilvGMEDA operon). It is therefore likely that...corresponding ilv locus was cloned from a gene of the chromosomal gene bank of S. **typhi** TY2 described in Example 9 by complementation of the E. coli K-12 ilvC **mutant** strain AB1419. The ilvC locus is adjacent to the ilvGMEDA operon in the E. coli ...

...not pILV18, also complemented the ilv defect of both the E. coli K-12 ilvD **mutant** strain AB1280 and S. **typhi** TY21a. This shows that clone pILV12, but not pILV18, most likely includes both the ilvGMEDA...

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29oct02 11:19:39 User228206 Session D1877.4

$0.21 0.066 DialUnits File155
$0.42 2 Type(s) in Format 9
$0.42 2 Types
$0.63 Estimated cost File155
$1.89 0.111 DialUnits File357
$13.50 5 Type(s) in Format 3
$13.50 5 Types
$15.39 Estimated cost File357
$0.10 0.011 DialUnits File73
$0.10 Estimated cost File73
$0.06 0.011 DialUnits File5
$0.06 Estimated cost File5
$0.59 0.100 DialUnits File652
$0.70 1 Type(s) in Format 3
$0.70 1 Types
$1.29 Estimated cost File652
$0.05 0.011 DialUnits File50
$0.05 Estimated cost File50
$0.05 0.011 DialUnits File35
$0.05 Estimated cost File35
$0.04 0.011 DialUnits File370
$0.04 Estimated cost File370
$0.17 0.044 DialUnits File65
$2.20 2 Type(s) in Format 9
$2.20 2 Types
$2.37 Estimated cost File65
$0.30 0.011 DialUnits File128
$0.30 Estimated cost File128
$0.48 0.089 DialUnits File16
$10.35 3 Type(s) in Format 9
$10.35 3 Types
$10.83 Estimated cost File16
$0.91 0.199 DialUnits File348
$1.70 1 Type(s) in Format 3
$1.70 1 Types
$2.61 Estimated cost File348
OneSearch, 12 files, 0.675 DialUnits FileOS
$0.21 TELNET
$33.93 Estimated cost this search
$33.93 Estimated total session cost 0.675 DialUnits

### Status: Signed Off. (1 minutes)

WEST

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L2: Entry 1 of 3 File: USPT Oct 22, 2002

US-PAT-NO: 6468739
DOCUMENT-IDENTIFIER: US 6468739 B1

TITLE: Process for identifying secretory genes from helicobacter pylori

DATE-ISSUED: October 22, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Haas; Rainer | Munchen | | | DE |
| Odenbreit; Stefan | Munchen | | | DE |
| Meyer; Thomas | Tubingen | | | DE |

US-CL-CURRENT: 435/6; 435/320.1, 435/69.1, 435/69.8, 536/23.1, 536/23.7

CLAIMS:

What is claimed is:

1. A method for identifying a Helicobacter pylori gene which codes for a protein having secretory activity, the method comprising the steps of: (a) providing a prokaryotic host cell which contains (1) a transposon inducible in the host cell coupled to a marker for secretory activity and (2) a library of minimal plasmid vectors comprising (i) an expression control sequence active in the host cell and (ii) a H. pylori DNA library which may contain a gene which codes for a protein having secretory activity, wherein the H. pylori DNA is operatively linked to the expression control sequence; (b) inducing the insertion of the transposon into the H. pylori DNA; and (c) identifying any H. pylori gene which codes for a protein having secretory activity, by detecting the marker.

2. The method of claim 1, wherein the H. pylori DNA library contains over 90% of the H. pylori genome.

3. The method of claim 1, wherein the host cell is an E. coli cell.

4. The method of claim 1, wherein the H. pylori DNA library contains a gene which codes for a protein having secretory activity, step (b) comprises inducing the insertion of the transposon into the gene to produce a mutated H. pylori gene which codes for a fusion protein having secretory activity, and step (c) comprises expressing the mutated H. pylori gene in the host cell, whereby the fusion protein is secreted by the host cell and the marker is displayed.

5. The method of claim 1, wherein the gene codes for a protein having adhesin

activity.

6. The method of claim 1, wherein the vector is pMin2 (DSM 10007).

7. The method of claim 1, wherein the marker is a .beta.-lactamase gene without a signal sequence.

8. The method of claim 1, wherein the transposon is TnMax9 (DSM 10008).

9. The method of claim 1, wherein the minimal plasmid vector further comprises (iii) a sequence which enables a conjugative transfer of DNA into a prokaryotic receiver cell, and the method further comprises, between step (b) and step (c), conjugatively transferring the H. pylori DNA containing the transposon from the host cell into the receiver cell, and wherein step (c) is conducted in the receiver cell.

10. The method of claim 9, wherein the receiver cell is an E. coli cell.

11. A method for identifying a Helicobacter pylori gene which codes for a protein having secretory activity and adherence activity, comprising the steps of: (a) providing a prokaryotic host cell which contains (1) a transposon inducible in the host cell coupled to a marker for secretory activity and (2) a library of minimal plasmid vectors comprising (i) an expression control sequence active in the host cell and (ii) a H. pylori DNA library which contains a gerie which codes for a protein having secretory activity and adhesin activity, wherein the H. pylori DNA is operatively linked to the expression control sequence; (b) inducing the insertion of the transposon into the H. pylori DNA; (c) identifying a H. pylori gene which codes for a protein having secretory activity, by detecting the marker; (d) transforming the H. pylori gene from step (c) into H. pylori and integrating the H. pylori gene into the H. pylori genome to produce an isogenic H. pylori mutant strain; and (e) screening the isogenic H. pylori mutant strain for adherence deficiency, thereby identifying a H. pylori gene which codes for a protein having secretory activity and adherence activity.

12. The method of claim 11, wherein the H. pylori DNA library contains over 90% of the H. pylori genome.

13. The method of claim 11, wherein the host cell is an E. coli cell.

14. The method of claim 11, wherein the vector is pMin2 (DSM 10007).

15. The method of claim 11, wherein the marker is a .beta.-lactamase gene without a signal sequence.

16. The method of claim 11, wherein the transposon is TnMax9 (DSM 10008).

17. The method of claim 11, wherein the minimal plasmid vector further comprises (iii) a sequence which enables a conjugative transfer of DNA into a prokaryotic receiver cell, and the method further comprises, between step (b) and step (c), conjugatively transferring the H. pylori DNA containing the transposon from the host cell into the receiver cell, and wherein step (c) is conducted in the receiver cell.

18. The method of claim 17, wherein the receiver cell is an E. coli cell.

19. The method of claim 11, wherein said step (e) comprises screening the isogenic H. pylori mutant strain for adherence deficiency with respect to epithelial cells.

20. A prokaryotic host cell which contains (1) a transposon inducible in the host cell coupled to a marker for secretory activity and (2) a library of minimal plasmid vectors comprising (i) an expression control sequence active in the host cell and (ii) a H. pylori DNA library which contains a gene which codes for a protein having secretory activity, wherein the H. pylori DNA is operatively linked to the expression control sequence, and wherein at least 90% of the H.

pylori genome is contained in the DNA library.

21. The host cell of claim 20, wherein the host cell is an E. coli cell.

22. The host cell of claim 20, wherein the H. pylori DNA library is composed of gene fragments having an average size of 3-6 kbases.

23. The host cell of claim 20, wherein the DNA library contains at least 400 independent clones.

**New** Helicobacter **antigenic preparation - recombinant antigen production by vector plasmid expression in Escherichia coli, and corresponding monoclonal antibody, for application as a recombinant vaccine**

AUTHOR: Doidge C V; Lee A; Radcliffe F J; Hocking D M; Webb E A
CORPORATE SOURCE: Parkville, Victoria, Australia; Kensington, New South Wales, Australia.

PATENT ASSIGNEE: CSL; Univ.New-South-Wales 1996
PATENT NUMBER: WO 9633220 PATENT DATE: 961024 WPI ACCESSION NO.: 96-485735 (9648)
PRIORITY APPLIC. NO.: AU 967565 APPLIC. DATE: 960116
NATIONAL APPLIC. NO.: WO 96AU225 APPLIC. DATE: 960419
LANGUAGE: English

**New** Helicobacter **antigenic preparation**

...ABSTRACT: are claimed: 1) an antigen preparation (AP), for use in the treatment of prevention of **Helicobacter** sp. infection in a human host, comprising antigens of mol.wt. 19,000 (a), 13...

...000 (d), and 29,000 (e), respectively (the preparation may also comprise at least one **Helicobacter pylori** or **Helicobacter** felis antigen); 2) antigens (a)-(e); 3) a vaccine comprising an immunologically effective amount of...

... molecule of 7); 9) Escherichia coli transformed with the vector of 8); and 10) a **recombinant** polypeptide expressed in the host cell of 9). Nucleic acids may be used in plasmids as vaccine vectors ( **Salmonella** , Shigella, Yersinia, Vibrio, Escherichia, or BCG) expressing the antigens in a host. (86pp)

DESCRIPTORS: **Helicobacter** sp. recombinant antigen prep., vector plasmid expression in Escherichia coli, monoclonal antibody, appl. recombinant vaccine...